



10-761593-revised-a.ST25  
SEQUENCE LISTING



<110> Sun, Lee-Hwei K  
Sun, Bill N  
Sun, Cecily R

<120> Fc fusion proteins of human erythropoietin with high biological activities

<130> 02SUN2001-A

<140> US 10/761,593

<141> 2004-01-21

<150> 09/932812

<151> 2001-08-17

<160> 28

<170> PatentIn version 3.2

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 ttgtgtcga

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<212> DNA  
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 agccgagtcc tggagaggta cctcttggag gccaaggagg ccgagaatat cacgacgggc 180  
 tgtgctgaac actgcagctt gaatgagaat atcactgtcc cagacaccaa agttaatttc 240  
 tatgcctgga agaggatgga ggtcgggcag caggccgtag aagtctggca gggcctggcc 300  
 ctgctgtcgg aagctgtcct gcggggccag gccctgttgg tcaactcttc ccagccgtgg 360  
 gagcccctgc agctgcatgt ggataaagcc gtcagtggcc ttcgcagcct caccactctg 420  
 cttcgggctc tgggagccca gaaggaagcc atctcccctc cagatgcggc ctcagctgct 480  
 ccactccgaa caatcactgc tgacactttc cgaaaactct tccgagtcta ctccaatttc 540  
 ctccggggaa agctgaagct gtacacaggg gaggcctgca ggacagggga cggatccggt 600  
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 cccaaggaca ccctcatgat ctcccggacc cctgagggtca cgtgcgtggg ggtggacgtg 780  
 agccacgaag accccgaggt ccagttcaac tggtagctgg acggcgtgga ggtgcataat 840  
 gccaagacaa agccacggga ggagcagttc aacagcacgt tccgtgtggg cagcgtcctc 900  
 accgttgtgc accaggactg gctgaacggc aaggagtaca agtgcaaggt ctccaacaaa 960  
 ggcctcccag cctccatcga gaaaaccatc tccaaaacca aagggcagcc ccgagaacca 1020  
 cagggtgtaca ccctgcccc atcccgggag gagatgacca agaaccaggt cagcctgacc 1080  
 tgcctgggtca aaggcttcta cccagcgac atcgccgtgg agtgggagag caatgggcag 1140  
 ccggagaaca actacaagac cacacctccc atgctggact ccgacggctc cttcttcctc 1200  
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gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt 1320  
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<210> 18  
 <211> 436  
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 <213> Artificial Sequence

<220>  
 <223> HuEPO-L-vFc gamma2 with a 27-amino acid leader peptide (Figure 2A)

<400> 18

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu  
 1 5 10 15

Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu  
 20 25 30

Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu  
 35 40 45

Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu  
 50 55 60

Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg  
 65 70 75 80

Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu  
 85 90 95

Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser  
 100 105 110

Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly  
 115 120 125

Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu  
 130 135 140

Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile  
 145 150 155 160

Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu  
 165 170 175

Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp  
 180 185 190

Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
195 200 205

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val  
210 215 220

Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu  
225 230 235 240

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser  
245 250 255

His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu  
260 265 270

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr  
275 280 285

Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn  
290 295 300

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Ser  
305 310 315 320

Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln  
325 330 335

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val  
340 345 350

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val  
355 360 365

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro  
370 375 380

Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr  
385 390 395 400

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val  
405 410 415

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu  
420 425 430

Ser Pro Gly Lys

435

<210> 19  
 <211> 1335  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> HuEPO-L-vFc gamma4 (Figure 2B)

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 ctgctgtcgc tccctctggg cctcccagtc ctgggcgccc caccacgcct catctgtgac 120  
 agccgagtcc tggagaggtta cctcttggag gccaaggagg ccgagaatat cagcaggggc 180  
 tgtgtgaac actgcagctt gaatgagaat atcactgtcc cagacaccaa agttaatttc 240  
 tatgcctgga agaggatgga ggtcgggcag caggccgtag aagtctggca gggcctggcc 300  
 ctgctgtcgg aagctgtcct gcggggccag gccctgttgg tcaactcttc ccagccgtgg 360  
 gagccccctgc agctgcatgt ggataaagcc gtcagtggcc ttcgcagcct caccactctg 420  
 cttcgggctc tgggagccca gaaggaagcc atctcccctc cagatgcggc ctcagctgct 480  
 ccactccgaa caatcactgc tgacactttc cgcaaactct tccgagtcta ctccaatttc 540  
 ctccggggaa agctgaagct gtacacaggg gaggcctgca ggacagggga cggatccggt 600  
 ggcggttccg gtggaggcgg aagcggcggt ggaggatcag agtccaaata tggccccca 660  
 tgcccaccat gcccagcacc tgagttcgcg gggggaccat cagtcttcct gttccccca 720  
 aaaccaagg acactctcat gatctcccgg acccctgagg tcacgtgcgt ggtggtggac 780  
 gtgagccagg aagaccccga ggtccagttc aactggtacg tggatggcgt ggaggtgcat 840  
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 aaaggcctcc cgtcctccat cgagaaaacc atctccaaag ccaaaggga gccccgagag 1020  
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 cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctcttcttc 1200  
 ctctacagca ggctaaccgt ggacaagagc aggtggcagg aggggaatgt cttctcatgc 1260  
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<210> 20  
 <211> 437  
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 <213> Artificial Sequence



<220>  
<223> HuEPO-L-vFc gamma4 with a 27-amino acid leader peptide (Figure 2B)

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1 5 10 15

Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu  
20 25 30

Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu  
35 40 45

Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu  
50 55 60

Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg  
65 70 75 80

Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu  
85 90 95

Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser  
100 105 110

Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly  
115 120 125

Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu  
130 135 140

Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile  
145 150 155 160

Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu  
165 170 175

Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp  
180 185 190

Gly ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
195 200 205

Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe  
210 215 220

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Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr  
225 230 235 240

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val  
245 250 255

Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val  
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser  
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu  
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser  
305 310 315 320

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro  
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln  
340 345 350

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala  
355 360 365

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr  
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu  
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser  
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser  
420 425 430

Leu Ser Leu Gly Lys  
435

<210> 21  
<211> 1329  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> HuEPO-L-VFC gamma1 (Figure 2C)

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agccgagtcc tggagaggta cctcttggag gccaaggagg ccgagaatat cacgacgggc 180
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tatgcctgga agaggatgga ggtcgggcag caggccgtag aagtctggca gggcctggcc 300
ctgctgtcgg aagctgtcct gcggggccag gccctgttgg tcaactcttc ccagccgtgg 360
gagcccctgc agctgcatgt ggataaagcc gtcagtggcc ttcgcagcct caccactctg 420
cttcgggctc tgggagccca gaaggaagcc atctcccctc cagatgcggc ctcagctgct 480
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gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggcttc caacaaagcc 960
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gtgtacaccc tgccccatc ccgggatgag ctgaccaaga accagggtcag cctgacctgc 1080
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gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1200
agcaagctca ccgtggacaa gagcagggtg cagcagggga acgtcttctc atgctccgtg 1260
atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 1320
tgagaattc 1329

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<213> Artificial Sequence

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                   20                                  25                                  30  
 Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu  
           35                                  40                                  45  
 Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu  
           50                                  55                                  60  
 Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg  
   65                                  70                                  75                                  80  
 Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu  
                   85                                  90                                  95  
 Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser  
                   100                                  105                                  110  
 Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly  
           115                                  120                                  125  
 Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu  
   130                                  135                                  140  
 Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile  
  145                                  150                                  155                                  160  
 Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu  
                   165                                  170                                  175  
 Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp  
                   180                                  185                                  190  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
           195                                  200                                  205  
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Val Ala Gly  
   210                                  215                                  220  
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met  
  225                                  230                                  235                                  240  
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His  
                   245                                  250                                  255  
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val  
           260                                  265                                  270

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His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr  
275 280 285

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly  
290 295 300

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile  
305 310 315 320

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val  
325 330 335

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser  
340 345 350

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu  
355 360 365

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro  
370 375 380

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val  
385 390 395 400

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met  
405 410 415

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser  
420 425 430

Pro Gly Lys  
435

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<220>  
<223> synthetic linker

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<210> 24  
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<213> Homo sapiens

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Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro  
1 5 10 15

<210> 25

<211> 10

<212> PRT

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<400> 25

Asp Lys Thr His Thr Cys Pro Pro Cys Pro  
1 5 10

<210> 26

<211> 232

<212> PRT

<213> Homo sapiens

<400> 26

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala  
1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro  
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val  
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val  
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln  
65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln  
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala  
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro  
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr  
130 135 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser  
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Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr  
165 170 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr  
180 185 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe  
195 200 205

ser cys ser val met his glu ala leu his asn his tyr thr gln lys  
210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys  
225 230

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<400> 27

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val  
1 5 10 15

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20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser

His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu  
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr  
65 70 75 80

Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn  
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro  
100 105 110

Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln  
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val  
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135

140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val  
 145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro  
 165 170 175

Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr  
 180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val  
 195 200 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu  
 210 215 220

Ser Pro Gly Lys  
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<210> 28  
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 <213> Homo sapiens

<400> 28

Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe  
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Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr  
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Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val  
 35 40 45

Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val  
 50 55 60

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser  
 65 70 75 80

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu  
 85 90 95

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser  
 100 105 110

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro  
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Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln  
130 135 140

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala  
145 150 155 160

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr  
165 170 175

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu  
180 185 190

Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser  
195 200 205

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser  
210 215 220

Leu Ser Leu Gly Lys  
225